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PAPER

Obesity and central fat pattern among Greenland Inuit and a general population of Denmark (Inter99): Relationship to metabolic risk factors

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OBJECTIVE: To investigate whether the obesity observed among the Inuit of Greenland and in a general Danish population was associated with the same degree of metabolic disturbances.
DESIGN: Comparison of data from two population-based cross-sectional surveys conducted in 1999–2001.
SUBJECTS: A total of 7892 individuals aged 30–60 y, 1108 Inuit participants from the Greenland Population study, and 6784 Danish participants in the Danish Inter99 study.
MEASUREMENTS: Height, weight, waist and hip circumference were measured, and BMI and waist-to-hip ratio were calculated. The participants received a standard 75 g OGTT. s-Triglyceride, s-HDL cholesterol, fasting and 2 h p-glucose and s-insulin were analysed. Blood pressure was measured. Information on lifestyle factors was obtained by a questionnaire and interview.
RESULTS: The Inuit had lower levels of 2-h glucose and insulin, blood pressure, triglyceride, and higher levels of HDL cholesterol than the Danish participants at any given level of obesity. Fasting glucose and fasting insulin levels within obesity categories were not different in the two populations. Adjustment for physical activity, smoking, school education, and alcohol consumption did not change these findings.
CONCLUSION: The trends in the association between obesity and metabolic effects among the Inuit and a Northern European population were the same, but the levels of the risk factors were significantly different. This may be due to genetic factors and differences in body composition.
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Keywords: inuit; greenland; insulin resistance; metabolic disorder; anthropometric variables; body constitution

Introduction

Obesity has become an increasing public health problem because of its high prevalence and associated morbidities such as diabetes and cardiovascular disease. Obesity is related to glucose intolerance, dyslipidaemia, and hypertension; the so-called Metabolic Syndrome. Although pathophysiologic mechanisms linking obesity to these abnormalities are not completely clarified, it is well known that visceral fat accumulation and insulin resistance contribute to these metabolic disturbances in obese people.[1,2] Over the past few decades, substantial lifestyle changes have occurred in many aboriginal populations in the world, leading to an epidemic of obesity and diabetes, possibly due to a genetic predisposition to insulin resistance and diabetes in these populations. Under traditional living conditions characterised by ‘feast or famine’, insulin resistance and accumulation of fat has been advantageous, but with easy access to high caloric, and high fat food this predisposition will lead to clinical insulin resistance, also known as the ‘thrifty’ genotype hypothesis.[3]

Since 1950, the Inuit populations in Greenland, Canada, and Alaska have undergone rapid sociocultural changes, such as urbanisation, declining dependence on subsistence hunting and fishing, and dietary changes from a sea

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mammal- and fish-based diet to a diet influenced by typical Western dietary habits.

Recent studies of the Inuit have shown high prevalences of diabetes,[4,5] placing the Inuit among those ethnic groups (Asian Indians, Mexican Hispanics) with the strongest susceptibility to diabetes in the world. A longitudinal study from Igloolik in Canada demonstrated increasing prevalence of obesity as a result of acculturation.[6] Although no longitudinal studies of obesity exists from Greenland, cross-sectional studies in the past decade indicated increasing prevalence of obesity,[7,8] particularly among women.

The rapid increase in diabetes prevalence among Inuit indicates that these people are more susceptible to lifestyle changes than European populations. The question is whether the other components of the Metabolic Syndrome are more prevalent among the Inuit compared with Europeans. Thus, assuming that obesity is the main cause of the Metabolic Syndrome, the aim of the present study is to assess whether the obesity observed among the Inuit of Greenland and in a general Danish population is associated with the same degree of metabolic disturbances as reflected in levels in p-glucose, insulin, high-density lipoprotein (HDL) cholesterol, triglyceride, and blood pressure.

Methods

Participants

Data were collected from March 1999 to April 2001, in random samples of adult Greenlanders. The total population of Greenland is 56 000 of which 90% are ethnic Greenlanders (Inuit). Genetically, Greenlanders are Inuit (Eskimos) with a substantial admixture of European, mainly Danish, genes. They are closely related to the Inuit and Yupik in Canada, Alaska, and Siberia. Until the 1950s, most Greenlanders made their living by hunting and fishing. Today, hunting and fishing are important leisure time activities, and traditional Greenlandic food makes up a significant proportion of the diet. Parallel to this modernisation, physical activity level has decreased and the consumption of alcohol and tobacco has increased. For the survey, three areas of West Greenland were chosen, that is, the capital (Nuuk, 13 500 inhabitants) with the most Westernised living conditions, four villages in a hunting district (Uummannaq, 230–277 inhabitants per village), and a small town with intermediate living conditions (Qasigiannguit, 1400 inhabitants). The target population was adults aged 30 y and above. In Nuuk, a random sample was drawn from the Central Population Register. In Qasigiannguit and Uummannaq, the entire Inuit population aged 30 y and over was invited to participate. Only Inuit defined as persons with at least one Inuit parent were included in the study.

For comparison, data from a Danish survey Inter99 were used. The Inter99 is a population-based randomised non-pharmacological intervention study for prevention of cardiovascular disease. A random sample of 13 016 individuals from the western part of Copenhagen County aged 30, 35, 40, 45, 50, 55, or 60 y was invited.

For all participants informed consent was obtained in writing and orally. The relevant Ethics Review Committee had approved the study.

Interviews and questionnaires

Only identical questions in the two survey questionnaires were included in the analyses. In Greenland, the survey questionnaires were available in Danish and Greenlandic and used by the participant according to language preference. The questionnaire contained information on age, gender, physical activity, smoking habits, alcohol consumption, and school education.

Participants rated their physical activity level during leisure time into three categories: sedentary; moderate; and heavy physical activity. School education was recorded as the grade completed. Smoking behaviour was categorised into current smokers, never smokers, and previous smokers. The weekly consumption of alcohol was reported and recoded into four categories: 0 drinks per week, 1–7 drinks per week, 8–14 drinks per week, and 15 or more drinks per week.

Physical measurements

Greenland Population study The participants underwent anthropometric measurements, blood samples, and a 75 g standardised oral glucose tolerance test (OGTT). Weight and height were measured with the participants wearing undergarments, and body mass index (BMI) was calculated. On the standing participant, waist circumference was measured midway between the iliac crest and the costal margin, hip circumference at its maximum.

Only those aged 35 y and above received an OGTT. Participants with known diabetes did not have an OGTT, but fasting venous plasma p-glucose was measured. Plasma samples were immediately put on ice and spun at 4°C within 30 min of sampling. Plasma glucose was determined by the hexokinase/G6P-DH method on a Hitachi 912 system. Glucose tolerance was classified according to the WHO criteria 1999.[9] The determination of serum insulin was made by enzyme-linked immunoassay, and the laboratory of the Steno Diabetes Centre, Denmark performed the analyses of plasma glucose and serum insulin. Serum-cholesterol was determined using enzymatic calorimetric techniques (Boehringer Mannheim, Germany). Analyses were performed at the Department of Clinical Chemistry, Bispebjerg Hospital, University of Copenhagen, Denmark. Three sitting blood pressures were measured using a standard mercury sphygmomanometer with an appropriate cuff size after at least 5 min rest. The mean of the two last blood pressures was calculated.

Inter99 study All participants underwent the same procedures as in the Greenland Population study. Plasma glucose and serum insulin were measured using the same methods and laboratory as used in the Greenland study. Serum cholesterol was analysed in the laboratory of Steno Diabetes Centre; however, the same method was used. In the Inter99 study, only two blood pressures were measured with the patient in lying position, and the mean of the two blood pressures was calculated.

Statistics and data analysis

Analyses were performed using SAS version 8.2 (SAS Institute, Carey, NC, USA). Analyses were run separately for men and women. Only participants within the same age range (30–60 y) were included in the analyses, and analyses of 2-h p-glucose and 2-h insulin were restricted to those aged 35 y and above. Means (s.d.) and proportions of baseline characteristics were compared by ethnic group using *t*-tests and χ^2 tests, respectively. Fasting and 2-h insulin were log-transformed and transformed back to geometric means for presentation. Age-adjusted means of insulin, p-glucose, blood pressure, and lipids by category of BMI, waist-to-hip ratio (WHR), and waist circumference were calculated in general linear models. Obesity measurements (waist circumference, WHR, and BMI) were analysed as independent variables in general linear models with each of the metabolic risk factors as dependent variable in the two populations. Only data on the relationship between waist circumference and the eight risk factors are shown in the figures, as waist circumference is suggested to be the best marker of intra-abdominal fat.

To test whether ethnicity modified the association between obesity and metabolic risk factors, we used an interaction term between ethnicity and BMI, WHR, and waist circumference, respectively. The following potential confounding factors were included as covariates in the linear models: physical activity, smoking, school education, and alcohol consumption. Subjects treated with antihypertensive or lipid-lowering medication were excluded from analyses of blood pressure and lipids, respectively. Persons with known diabetes were excluded from analyses that included p-glucose and insulin, due to the possibility that lifestyle changes or glucose-lowering agents may influence the levels of glucose and insulin as a function of obesity levels.

Results

The study population in Greenland and in Inter99 studies included 1108 Greenlanders and 6784 Danes aged 30–60 y. In Greenland, the mean age was 47.3 y compared to 46.0 y in Denmark ($P = 0.001$). In Greenland, 56.3% were female subjects compared to 51.3% in Denmark ($P = 0.005$).

Means of cardiovascular risk factors for each population are shown in Table 1. Despite having the highest means of BMI, waist-to-hip ratio, and waist circumference and higher prevalence of overall and central obesity, Inuit women had lower 2-h-glucose, 2-h insulin, blood pressure, triglyceride, and higher HDL cholesterol. A similar disparity prevailed in men with the exception of means of BMI and waist circumference, which were higher among Danish men. Inuit of either sex had a higher prevalence of diabetes.

To investigate further the differences in p-glucose and insulin levels between the two ethnic groups, means for each risk factor were computed within categories of waist circumference (Figure 1). The fasting p-glucose did not differ across ethnic groups. Both fasting p-glucose and 2-h

Table 1 Characteristics of the two populations by gender. Means with sd

	Men			*Women*		
	Greenland	*Denmark*	P-*value*	*Greenland*	*Denmark*	P-*value*
n	485	3302		623	3482	
Age (y)	47.6 (12.1)	46.4 (7.9)	0.069	47.0 (12.4)	45.7 (8.0)	0.01
BMI (kg/m^2)	26.3 (4.4)	26.8 (4.0)	0.03	26.8 (5.4)	25.9 (5.1)	0.01
WHR (%)	0.94 (0.07)	0.92 (0.06)	<0.001	0.89 (0.08)	0.80 (0.06)	<0.001
Waist circumference (cm)	90.9 (11.9)	93.3 (11.0)	0.001	87.9 (13.3)	79.8 (14.6)	<0.001
% obese[a]	18.4	17.7	0.74	24.9	17.8	0.001
% with abdominal obesity[b]	15.9	8.3	<0.001	58.1	17.7	<0.001
Fasting glucose (mmol/l)	5.9 (0.9)	5.8 (1.2)	0.86	5.8 (1.4)	5.4 (1.1)	<0.001
2-h glucose (mmol/l)	5.1 (2.2)	6.3 (2.5)	<0.001	6.1 (2.9)	6.3 (2.0)	0.09
Fasting insulin (pmol/l)	37 (2.0)	37 (1.9)	0.6	42 (1.9)	34 (1.8)	<0.001
2-h insulin (pmol/l)	53 (2.8)	138 (2.5)	<0.001	112 (2.5)	173 (2.1)	<0.001
% with diabetes	10.7	7.8	0.04	8.9	5.8	0.004
SBP (mmHg)	119 (17.1)	134 (16.6)	<0.001	117 (17.8)	127 (17.8)	<0.001
DBP (mmHg)	75 (11.6)	85 (10.9)	<0.001	72 (11.1)	80 (11.1)	<0.001
% with hypertension[c]	11.4	32.9	<0.001	9.5	22.8	<0.001
Triglyceride (mmol/l)	1.1 (0.6)	1.6 (0.4)	<0.001	1.1 (0.4)	1.2 (0.4)	0.17
HDL cholesterol (mmol/l)	1.6 (0.5)	1.3 (0.4)	<0.001	1.60 (0.44)	1.55 (0.40)	0.02

[a]Defined as BMI $\geq$30 kg/m^2.
[b]Defined as waist circumference >88 cm for women and >102 cm for men.[9]

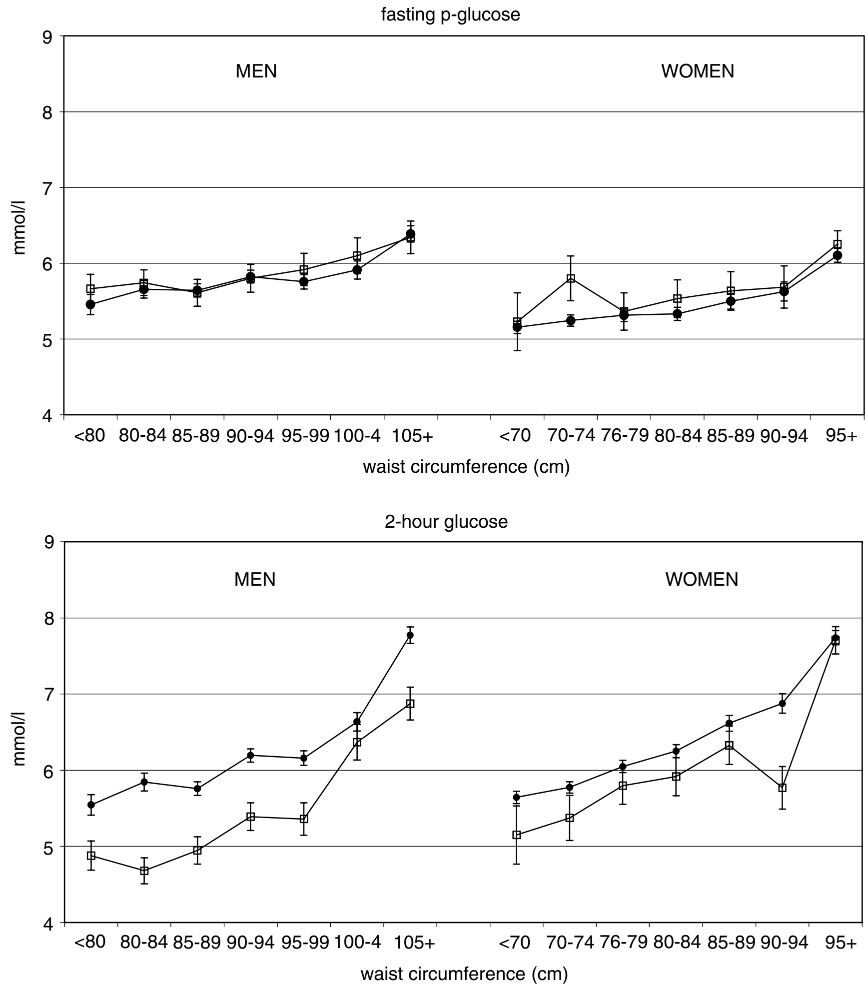

Figure 1 Means and 95% CIs of fasting and 2-h p-glucose by category of waist circumference and ethnicity. Age-adjusted values. Circles = Denmark, squares = Greenland.

p-glucose levels increased with increasing waist circumference in both populations, but in each category of waist circumference, Danish men and women had higher levels of 2-h p-glucose. The fasting and 2-h insulin curves were similar to those of p-glucose (Figure 2).

Figure 3 shows that both the Inuit women and men had significantly higher levels of HDL cholesterol than the Danish women in all but two groups of waist circumference. The levels of triglyceride were significantly lower in Inuit in most waist categories.

Finally, the Inuit consistently had the lowest levels of both systolic and diastolic blood pressure regardless of waist category (Figure 4).

Table 2 shows the age-adjusted regression parameter estimates for waist circumference, BMI, and WHR in a general linear model with each of the eight risk factors as dependent variables in the two populations. These data showed that the waist circumference, BMI, and WHR were less strongly associated with blood pressure and lipids in Inuit compared to Danes. Waist circumference and BMI were strongly associated with fasting p-glucose and less strongly associated with 2-h p-glucose in Inuit female subjects compared to Danish female subjects, while no significant difference in the association between WHR and p-glucose was seen in the two populations. In Inuit women, WHR predicted lower levels of 2-h insulin than in Danish women, whereas ethnicity did not influence this association in men, neither the association between insulin and BMI and waist circumference, respectively. To test whether this influence of ethnicity was attenuated by lifestyle factors, the following confounders were included in the linear models: physical activity, smoking, school education, and alcohol consumption (data not shown). This did not change the significance of the interaction terms. Only in female subjects, the influence of ethnicity on the association between BMI and 2-h p-glucose was attenuated after adjustment for confounders. However, although statistically significant, the observed differences between the regression coefficients in

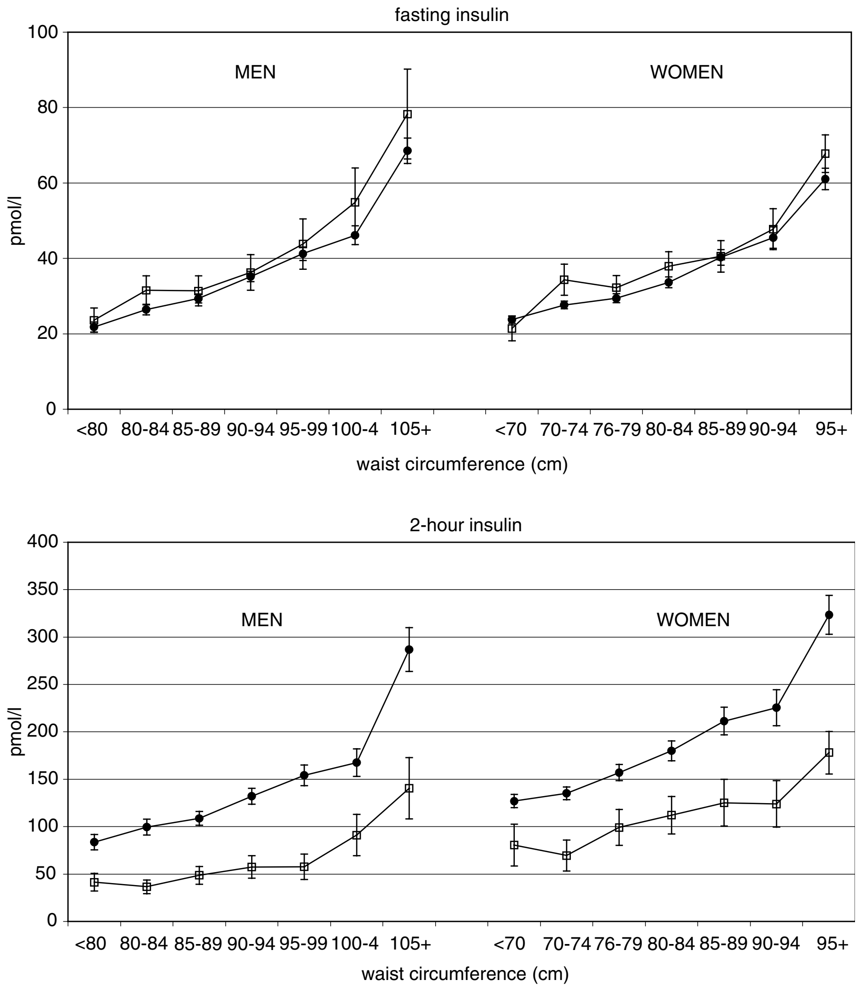

Figure 2 Geometric means and 95% CIs of fasting and 2-h insulin by category of waist circumference and ethnicity. Age-adjusted values. Circles-Denmark, squares = Greenland.

Table 2 were small from a clinical point of view. Thus, the main differences between the populations seem to be due to differences in levels of metabolic risk factors and not to differences in the effect of obesity.

In secondary analyses, we excluded individuals treated with hormone replacement therapy. This did not alter the results.

Discussion

We found that the Inuit had lower levels of 2-h p-glucose and insulin, blood pressure, triglyceride, and higher levels of HDL cholesterol than the Danish participants at any given level of obesity, even though there was generally an increasing trend in levels of metabolic risk factors with obesity in both populations. Thus, our data could not confirm the 'thrifty' genotype hypothesis among the Inuit of Greenland.

Only fasting p-glucose and fasting insulin levels with obesity categories were not different in the two populations. The paradox arising from this observation, given the high prevalence of diabetes in Greenland, may be attributable to a genetic disposition among the Inuit to deficiency in insulin secretion, rather than insulin resistance. Recent studies have shown that elevated values of fasting glucose are associated with a more pronounced defect in early insulin secretion and increased endogenous glucose output compared with elevated 2-h glucose values.[10,11]

There were some methodological differences between the two studies. Lipid analyses were performed at two different laboratories in Copenhagen County. However, the same method was used, and the two laboratories used the same calibrators, and followed the same quality assurance programme. In the Danish survey, blood pressure was measured with the participant in lying position. Since blood pressure is lower in lying position, this method should tend to underestimate the difference in blood pressure in the two surveys.

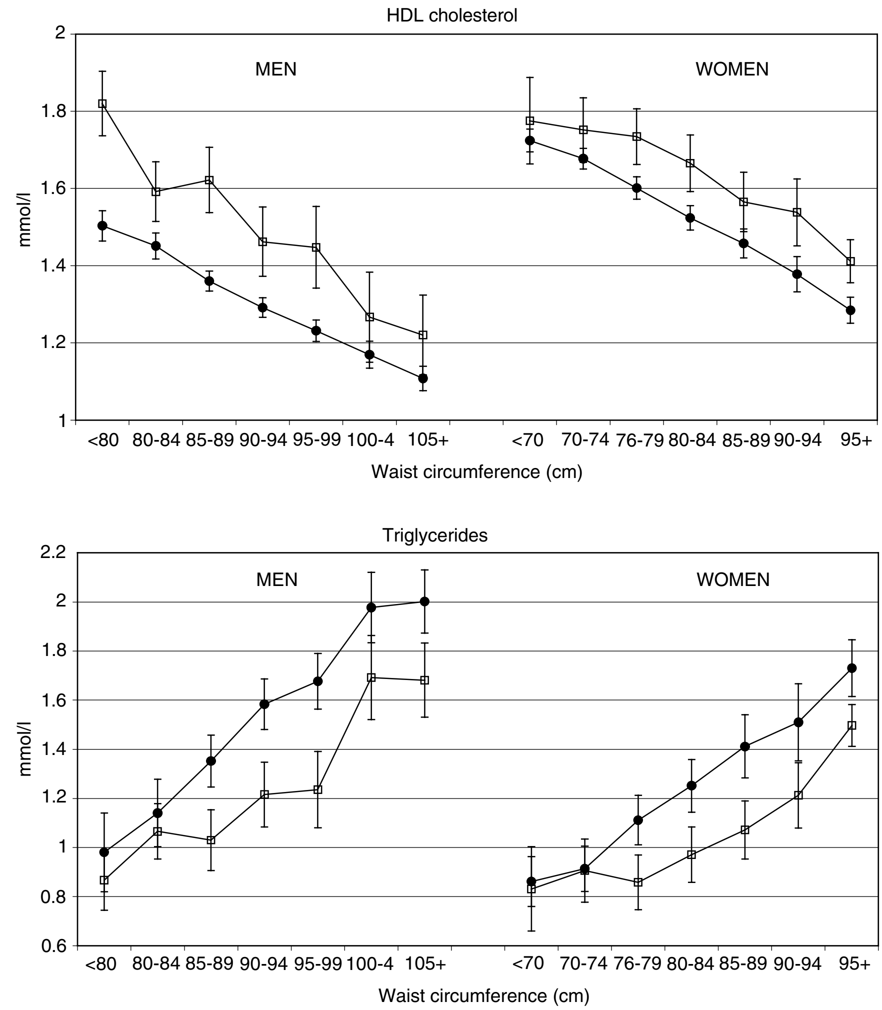

Figure 3 Means and 95% CIs of HDL cholesterol and triglyceride by category of waist circumference and ethnicity. Age-adjusted values. Circles = Denmark, squares = Greenland.

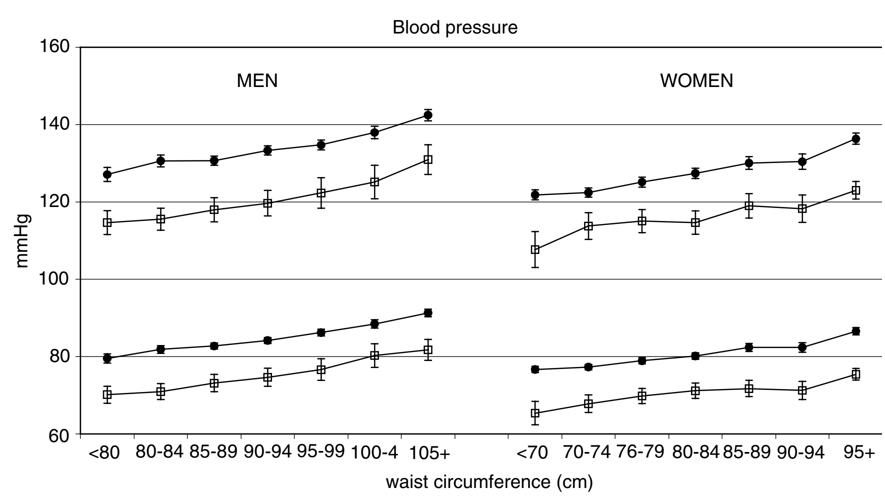

Figure 4 Means and 95% CIs of systolic blood pressure (upper lines) and diastolic blood pressure (lower lines) by category of waist circumference and ethnicity. Age-adjusted values. Circles = Denmark, squares = Greenland.

Table 2 Linear regression coefficients for waist circumference, BMI, and WHR as explanatory variables of eight metabolic risk factors in the two populations for men and women separately

	Glucose 0 (mmol/l)	*Glucose 120 (mmol/l)*	*Insulin 0 (%increase)*	*Insulin 120 (%increase)*	*SBP (mmHg)*	*DBP (mmHg)*	*HDL chol. (mmol/l)*	*Triglyceride (mmol/l)*
Waist circumference[a]								
Men								
Greenland	0.111	0.224	16.3	12.4	1.44	1.12	−0.047	0.116
Denmark	0.111	0.278	16.0	17.6	2.14	1.63	−0.058	0.136
P-value	*0.380*	*0.692*	*0.935*	*0.247*	*0.045*	*0.023*	*0.001*	*0.042*
Women								
Greenland	0.135	0.263	13.4	9.7	1.37	0.83	−0.052	0.094
Denmark	0.128	0.290	13.1	13.2	2.02	1.38	−0.058	0.105
P-value	*0.007*	*0.004*	*0.369*	*0.740*	*0.051*	*0.001*	*0.311*	*0.049*
BMI[b]								
Men								
Greenland	0.060	0.128	8.7	6.4	0.69	0.58	−0.025	0.060
Denmark	0.060	0.167	8.4	9.7	1.17	0.93	−0.033	0.075
P-value	*0.206*	*b0.179*	*0.731*	*0.966*	*0.039*	*0.047*	*0.056*	*0.040*
Women								
Greenland	0.059	0.124	6.5	4.7	0.69	0.41	−0.024	0.038
Denmark	0.048	0.129	5.9	6.2	1.04	0.72	−0.026	0.40
P-value	*0.013*	*0.003*	*0.389*	*0.338*	*0.172*	*0.052*	*0.669*	*0.480*
WHR[c]								
Men								
Greenland	0.158	0.359	20.7	14.8	2.00	1.15	−0.066	0.206
Denmark	0.163	0.427	21.7	20.3	1.79	1.72	−0.080	0.233
P-value	*0.339*	*0.928*	*0.765*	*0.311*	*0.065*	*0.002*	*0.055*	*0.006*
Women								
Greenland	0.195	0.420	17.0	15.4	1.25	0.59	−0.080	0.174
Denmark	0.198	0.473	17.4	20.1	1.93	1.14	−0.091	0.197
P-value	*0.924*	*0.255*	*0.662*	*0.005*	*0.012*	*0.0004*	*0.002*	*0.017*

[a]Comparison: each 5 cm increase.
[b]Comparison: each 1 unit increase.
[c]Comparison: each 5% increase.
Age is included as a continuous variable in the model. *P*-values are for the hypothesis of no differences between the coefficients.

Thus, it seems unlikely that methodological differences are responsible for the findings.

Obesity is thought to be an important determinant of metabolic risk factors. The results of this study suggest that genetic and/or behavioural factors associated with ethnicity may also contribute to these risk factors. This agrees with findings from previous cross-sectional studies.[12–16] Comparisons of the Inuit in Canada with a general North American population showed that the Inuit at each level of BMI had lower mean triglyceride and higher HDL cholesterol, whereas the association between glucose and insulin levels was similar in the two populations.[12] The NHANES III study found a weaker association between fasting insulin and BMI among black subjects when compared with white subjects.[13] Data from the San Antonio Heart Study revealed that the levels of glucose and insulin for a given level of BMI were higher in Mexican Americans compared with non-Hispanic whites. On the other hand, the levels of blood pressure for a given level of obesity were higher in white subjects.[14] The fact that Asian populations are experiencing high levels of diabetes at much lower levels of BMI than European populations has led to reassessment of the 'healthy range' of BMI for Asian populations by the WHO.[17]

Also, abdominal fatness has been shown to be less strongly associated with risk factors for CVD and type-II diabetes in black women than in white women.[18] A study from Mauritius found that Asian Indians had lower levels of HDL cholesterol and higher triglyceride levels at comparable levels of WHR compared with Creoles or Chinese.[19]

These population-specific differences in levels of insulin, glucose, blood pressure, and lipids presumably depend on an interaction between environmental factors and genetic factors that influence obesity and insulin sensitivity.

Living conditions are considerably different in Greenland and Denmark. However, differences in physical activity, smoking habits, and alcohol consumption could not explain the findings in our study. There may be other important environmental factors that influence the pattern of obesity. Owing to the differences in the questionnaires used, we were unable to analyse the impact of diet and socioeconomic status on obesity and metabolic risk factors in the two populations. Especially the traditional Greenlandic diet, which is rich in omega-3 polyunsaturated fatty acids, is suggested to contribute to the favourable cardiovascular risk profile.[7]

An alternative explanation is that anthropometrical measurements such as BMI, WHR, and waist circumference do not reflect the same amount of fat or the same pattern of fat distribution in different populations. It is well established that there are differences in the relationship between body fat and BMI in different populations.[20–22] These differences may be due to differences in body composition, as well as differences in energy intake and physical activity. Indeed, excess abdominal fat is more important as a cardiovascular risk factor than excess body fat *per se*.[23,24] There is not much information about the relationship between intra-abdominal adipose tissue and anthropometrical measurements, such as waist circumference and WHR, in different populations. Epidemiological studies have mainly used the WHR to estimate the proportion of abdominal adipose tissue.[25] However, magnetic resonance imaging and computed tomography showed that a simple measurement such as waist circumference is the best anthropometric correlate of the amount of visceral adipose tissue.[26] This has led to the inclusion of waist circumference as the only obesity criteria in a newly suggested definition of the metabolic syndrome.[27]

The WHO has defined critical waist circumference values of 102 cm for men and 88 cm for women.[25] However, the WHO waist approach has been developed in white men and women,[23] and its impact on metabolic factors should not uncritically be extrapolated to other ethnic groups. In a previous study of the same population, we defined the cutpoints for large waist circumferences as the 90% percentile for slim persons, that is, persons with a BMI below 23 kg/m^2. The cutpoints for high waist circumference were >86 cm (men) and >80 cm (women).[8] However, for the present interethnic comparison, we chose the WHO guidelines.

In summary, we found the same trends in the association between obesity and metabolic effects among the Inuit and a white population, but the levels of the risk factors were significantly different. This may be due to a combination of genetic and dietary factors and differences in body composition. Our data underline the need for longitudinal data on the association between obesity and cardiovascular disease in different populations; and additional studies of the relationship between anthropometric measurements and intra-abdominal fat by imaging techniques in different populations are clearly warranted.

Abbreviations

OGTT, oral; glucose tolerance test
BMI, body; mass index
WHR, waist-to-hip; ratio
HDL cholesterol, high-density; lipoprotein cholesterol

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